

CLAIMS

1. A variant hepatocyte growth factor (HGF) which is substantially incapable of binding a heparan sulphate proteoglycan but which is capable of binding to the HGF receptor wherein a positively-charged amino acid residue in the hairpin loop structure of wild-type HGF has been replaced with an amino acid residue with a negative charge for use in medicine.
2. A variant human hepatocyte growth factor (HGF) according to Claim 1 wherein at least amino acid residue R73 has been replaced by an amino acid residue with a negative charge for use in medicine.
3. A variant human hepatocyte growth factor (HGF) according to Claim 1 ~~or 2~~ wherein at least amino acid residue R76 has been replaced by an amino acid residue with a negative charge for use in medicine.
4. A variant human hepatocyte growth factor (HGF) according to <sup>claim 1</sup> ~~any one of the preceding claims~~ wherein both amino acid residues R73 and R76 have been replaced independently with an amino acid residue with a negative charge for use in medicine.
5. A variant human hepatocyte growth factor (HGF) comprising amino acid residue replacements R73E and R76E for use in medicine.

AMENDED SHEET

6. A variant human hepatocyte growth factor (HGF) comprising amino acid residue replacements R73E, R76E and R93E for use in medicine.
7. A variant human hepatocyte growth factor (HGF) comprising amino acid residue replacements R73E, R76E and K78E for use in medicine.
8. A variant human hepatocyte growth factor (HGF) consisting of human HGF with amino acid replacements R73E and R76E for use in medicine.
9. A variant human hepatocyte growth factor (HGF) consisting of human HGF with amino acid replacements R73E, R76E and R93E for use in medicine.
10. A variant human hepatocyte growth factor (HGF) consisting of human HGF with amino acid replacements R73E, R76E and K78E for use in medicine.
11. A variant hepatocyte growth factor (HGF) according to <sup>claim 1</sup> ~~any one of~~ ~~Claims 1 to 10~~ which antagonises the action of wild-type HGF for use in medicine.
12. A variant hepatocyte growth factor (HGF) according to Claim 11, wherein the variant HGF further comprises a mutation which confers resistance in the variant HGF to proteolytic cleavage by enzymes capable of *in vivo* conversion of HGF into its two-chain form for use in medicine.

13. A variant human hepatocyte growth factor (HGF) according to Claim 12 which have an amino acid alteration at or adjacent to any of amino acids 493, 494, 495 and 496 of the wild-type human HGF.
14. A pharmaceutical composition comprising a variant hepatocyte growth factor (HGF) as defined in <sup>claim 1</sup> ~~any of the preceding claims~~ and a pharmaceutically acceptable carrier.
15. A method of treating a patient in need of treatment with a hepatocyte growth factor or an antagonist thereof the method comprising administering to the patient an effective amount of a variant HGF as defined in <sup>claim 1</sup> ~~any one of Claims 1 to 13~~.
16. A method according to Claim 15 wherein the patient has cancer.
17. Use of a variant hepatocyte growth factor (HGF) as defined in <sup>claim 1</sup> ~~any one of Claims 1 to 10~~ in the manufacture of a medicament for treating a patient in need of treatment with a HGF or an antagonist thereof.
18. Use as defined in Claim 17 wherein the patient has cancer.
19. A variant hepatocyte growth factor (HGF) wherein a positively-charged amino acid residue in the hairpin loop structure of wild-type HGF has been replaced with an amino acid residue with a negative charge provided that the variant HGF is not a variant of human HGF in which the replacements (a) R73E, R76E and R93E

or (b) R73E and R76E or (c) K91E, R93E and K94E have been made.

20. A variant human hepatocyte growth factor (HGF) according to Claim 19 wherein at least amino acid residue R73 has been replaced by an amino acid residue with a negative charge.
21. A variant human hepatocyte growth factor (HGF) according to Claim 19 wherein at least amino acid residue R76 has been replaced by an amino acid residue with a negative charge.
22. A variant human hepatocyte growth factor (HGF) according to <sup>claim 19</sup> ~~any~~ ~~one of Claims 19 to 21~~ wherein both amino acid residues R73 and R76 have been replaced independently with an amino acid residue with a negative charge.
23. A variant human hepatocyte growth factor (HGF) comprising amino acid residue replacements R73E, R76E and K78E.
24. A variant hepatocyte growth factor (HGF) according to Claim 19 which antagonises the action of wild-type HGF.
25. A variant hepatocyte growth factor (HGF) according to Claim 24 wherein the variant HGF further comprises a mutation which confers resistance in the variant HGF to proteolytic cleavage by enzymes capable of *in vivo* conversion of HGF into its two chain form.

26. A variant human hepatocyte growth factor (HGF) according to Claim 25 which have an amino acid alteration at or adjacent to any of amino acids 493, 494, 495 and 496 of the wild-type human HGF.
27. A polynucleotide encoding a variant hepatocyte growth factor according to <sup>claim 19</sup> ~~any one of Claims 19 to 24~~.
28. A vector comprising a polynucleotide according to Claim 27.
29. A host cell comprising a polynucleotide or vector according to Claim 27 ~~or 28~~.
30. A method of producing a variant hepatocyte growth factor (HGF) the method comprising culturing a cell as defined in Claim 29 and isolating the variant HGF therefrom.
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